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Invited Commentary

The Emerging Role of Lipoprotein-associated Phospholipase A2 in Cerebrovascular Disease

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Previous studies have demonstrated increased serum levels of lipoprotein-associated phospholipase A2 (Lp-PLA2) in cardiovascular and cerebrovascular disease, including incident stroke,[1] and recurrent TIA or stroke.[2,3] Lp-PLA2 is an enzyme derived from inflammatory leukocytes involved in the metabolism of oxidized LDL by generating mediators (lysophosphatidylcholine and oxidized non-esterified fatty acids) involved in atherosclerotic plaque inflammation and formation of vulnerable (rupture-prone) and unstable (symptomatic) plaques rather than stimulation of atherogenesis.[4] Indeed, enhanced local expression of Lp-PLA2 in symptomatic carotid plaques has been reported.[5] In this issue, Sarlon-Bartoli went one step further by demonstrating increased serum Lp-PLA2 in ulcerated unstable atherosclerotic plaques and also a trend in unstable asymptomatic carotid plaques.[6] These findings have the potential to improve cerebrovascular disease stratification, however, correlation with ultrasonic or MRI markers of plaque instability or the presence of infarction on brain imaging was not performed.

Apart from its proposed use to refine primary and secondary risk stratification of coronary artery disease (CAD) by lowering LDL targets in moderate or high-risk patients,[7] (pending acceptance by the upcoming ATP III update), increased Lp-PLA2 levels have been suggested to appropriately classify previously misclassified persons who are actually at high risk of stroke and in need of aggressive stroke intervention.[8] Future studies could investigate the role of Lp-PLA2 on embolism during carotid stenting, or cerebrovascular risk stratification in longitudinal studies of patients with asymptomatic carotid stenosis. Certainly, positive results of the STABILITY trial, which investigates darapladib, an Lp-PLA2 inhibitor, in CAD,[9] could initiate a similar trial in patients with carotid stenosis.

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